Universitat Autònoma de Barcelona

FACULTAT DE VETERINÀRIA

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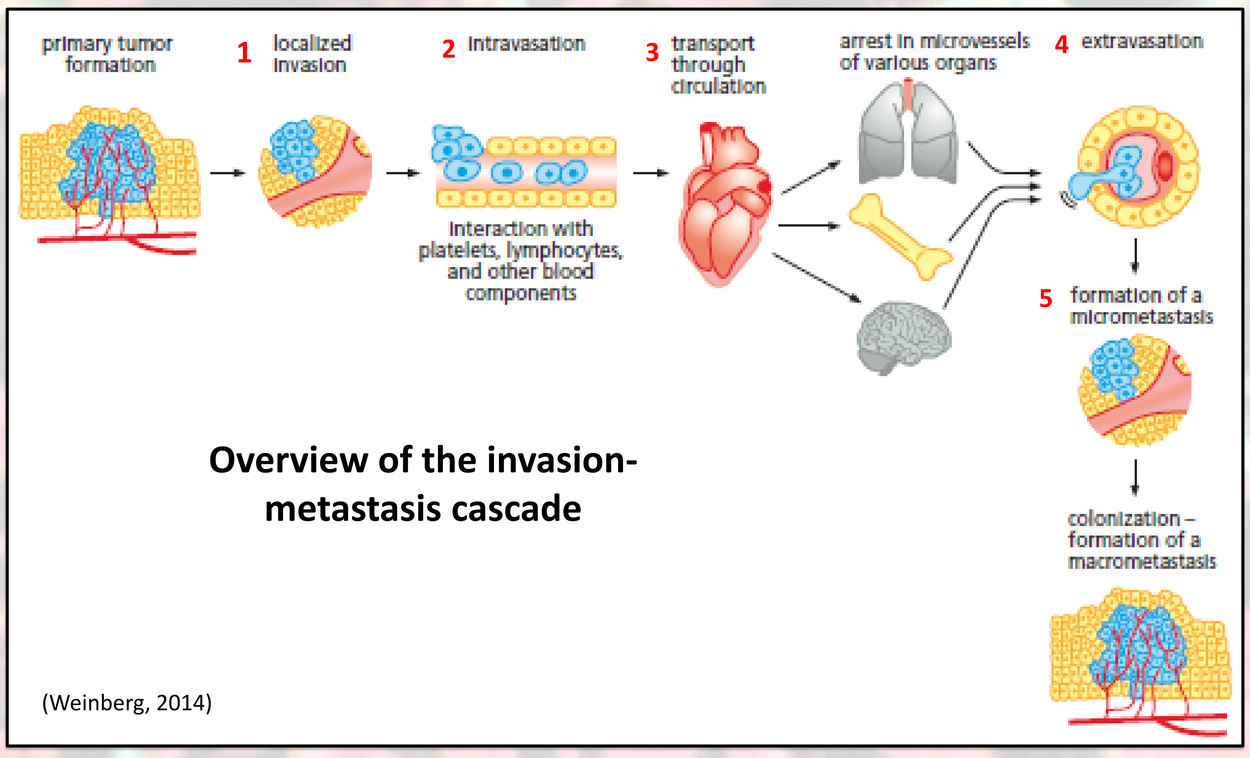
Final Degree Project

MOLECULAR BASIS OF TUMOR METASTASIS

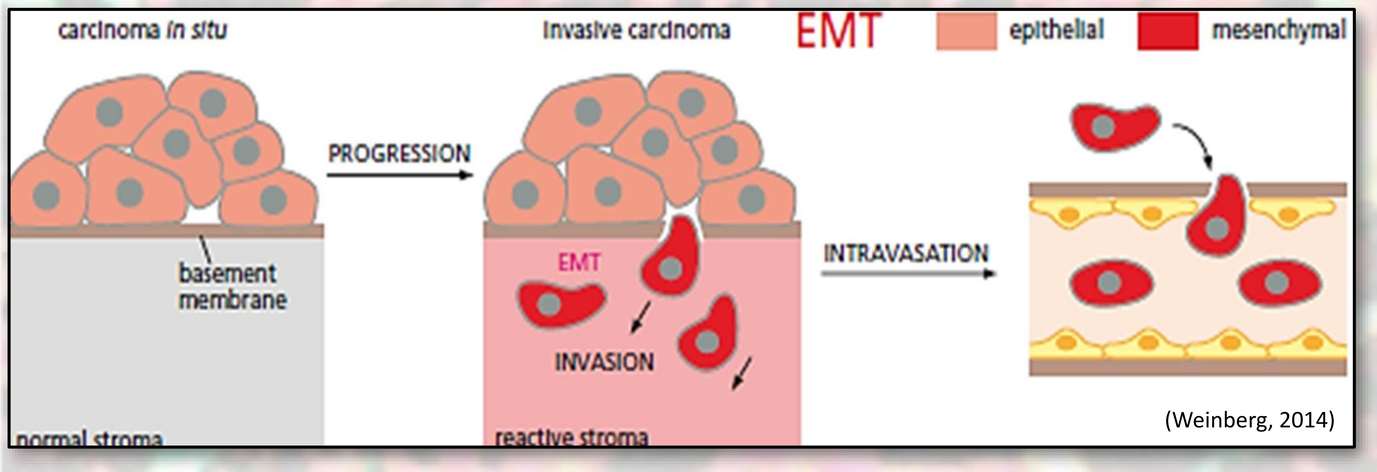
OBJECTIVES

- Explain and understand the different steps that conform the metastatic cascade.
- Understand the delicate equilibrium of this sequential process.
- Understand new therapies and where are they directed at.



Overview of the invasion-metastasis cascade

(Weinberg, 2014)



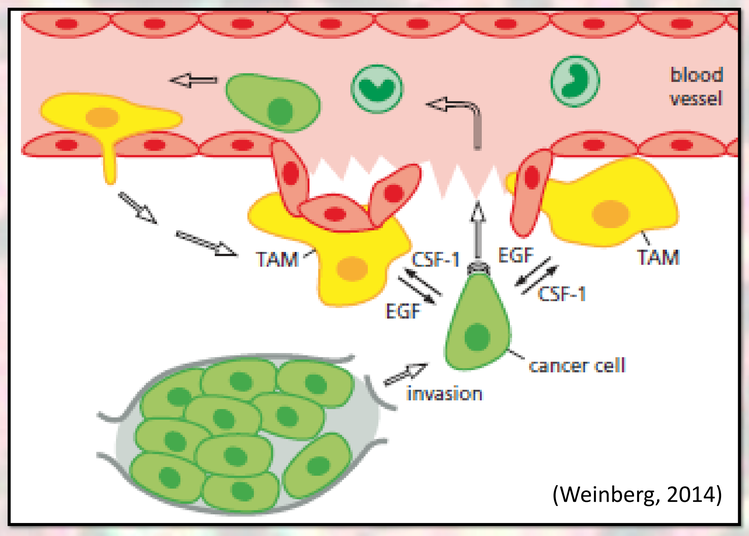
(Weinberg, 2014)

1.-EMT & INVASION

- Epithelial to mesenchymal phenotype
- E-cadherin → N-cadherin
- Mobility and migration
- Stromal signs & changes in gene expression
- Changes in cytoskeleton (lamellipodia)
- ECM degradation by MMP

2.-INTRAVASATION

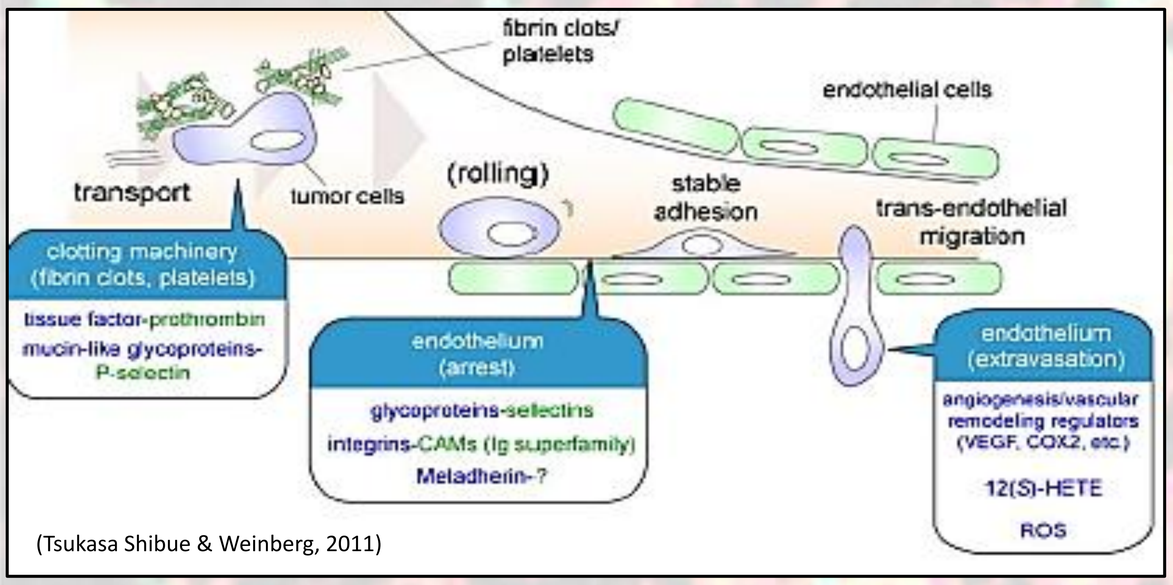
- Interactions between tumour cells, macrophages and endothelial cells
- Role of vascularization → VEGF, FGF (angiogenic factors)
- Less known step



(Weinberg, 2014)

3.-CIRCULATION

- Can be both lymphatic or hematogenous.
- Complex with fibrin & platelets → protection against stress and immune system.



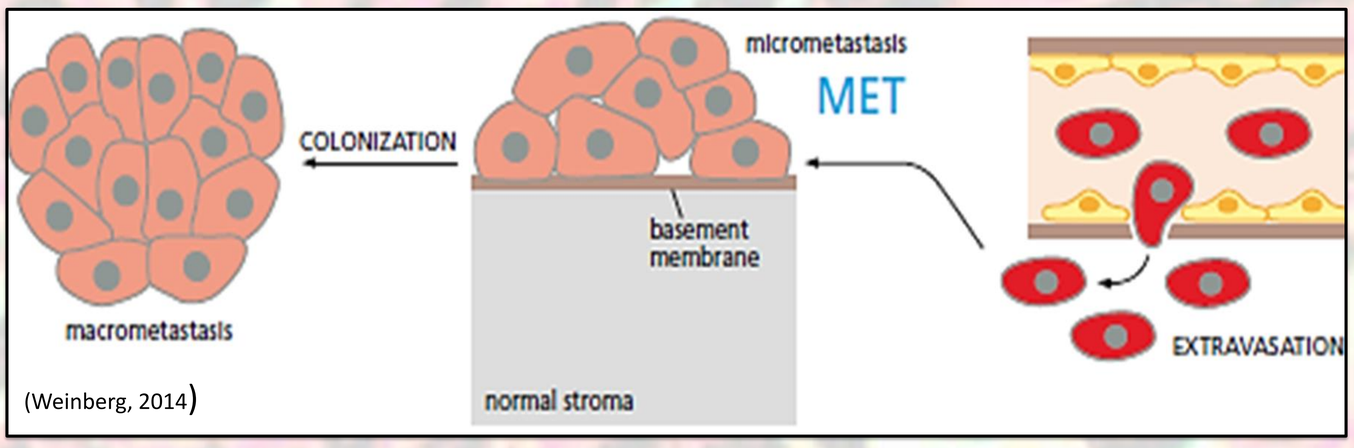
(Tsukasa Shibue & Weinberg, 2011)

4.-EXTRAVASATION

- Physical entrapment or specific interaction with endothelium
- Endothelial barrier modulation by ROS, [12(S)-HETE], VEGF, EGF…
- Platelets, macrophages, neutrophils and other cells may be involved.

5.-COLONIZATION

- Highly specialized
- Limiting step
- Low efficiency
- MET → mesenchymal to epithelial phenotype
- 3 destiny's : death, dormancy and macrometastasis
- Interactions between ECM, resident cells and other molecules.



(Weinberg, 2014)

CONCLUSIONS

- The invasive-metastasis cascade is formed by a combination of complex molecular processes.
- Synchronization is essential for this multistep process to occur.
- There are few therapies towards metastasis even though it is an important prognosis determinant for cancer patients